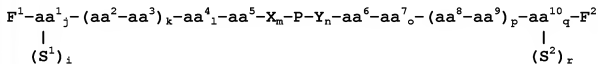


AMENDMENTS TO THE CLAIMS

Claim 1 (Previously presented): A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



wherein, P is a peptide consisting of the amino acid sequence YVHDAPV (SEQ ID NO:210);

F¹ and F² are fluorophores and F¹ is attached to the amino terminal amino acid and F² is attached to the carboxyl terminal amino acid;

S¹ and S², when present, are peptide spacers ranging in length from 1 to about 50 amino acids and S¹, when present, is attached to the amino terminal amino acid and S², when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

aa¹ and aa¹⁰ are independently selected from the group consisting of lysine, ornithine and cysteine;

-aa²-aa³-, and -aa⁸-aa⁹- are independently selected from the group consisting of an amino acid or a dipeptide where said amino acid or dipeptide consist of amino acids selected from the group consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

aa⁵, aa⁴, aa⁶, and aa⁷ are independently selected from the group consisting of proline, 3,4-dehydropyrolidine, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, βAla-Gly, βAla-βAla, γAbu-Gly, βAla-γAbu, Gly-Gly-Gly, γAbu-γAbu, Ahx-Gly, βAla-Gly-Gly, Ahx-βAla, βAla-βAla-Gly, Gly-Gly-Gly-Gly (SEQ ID NO:211), Ahx-γAbu, βAla-βAla-βAla, γAbu-βAla-Gly, γAbu-γAbu-Gly, Ahx-Ahx, γAbu-γAbu-βAla, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, Gly-βAla, βAla-βAla, Gly-γAbu, γAbu-βAla, Gly-Gly-Gly, γAbu-γAbu, Gly-Ahx, Gly-Gly-βAla, βAla-

Ahx, Gly- β Ala- β Ala, Gly-Gly-Gly-Gly (SEQ ID NO:211), γ Abu-Ahx, β Ala- β Ala- β Ala, Gly- β Ala- γ Abu, Gly- γ Abu- γ Abu, Ahx-Ahx, β Ala- γ Abu- γ Abu, and Gly-Ahx-Ahx; and

when i is 1, S¹ is joined to aa¹ by a peptide bond through a terminal alpha amino group of aa¹; and when r is 1, S² is joined to aa¹⁰ by a peptide bond through a terminal alpha carboxyl group of aa¹⁰.

Claim 2 (Original): The composition of claim 1, wherein the carboxyl terminal amino acid in which the carboxylic acid group is replaced with an amide.

Claim 3 (Previously presented): The composition of claim 1, wherein:

r is zero; and

aa¹⁰ has a C-terminal amide group or free carboxylic acid group.

Claim 4 (Previously presented): The composition of claim 1, comprising an amino acid sequence selected from the group consisting of KDPJGYVHDAPVGJPKGY (SEQ ID NO:171), and KDPYVHDAPVGJPKGY (SEQ ID NO:172).

Claim 5 (Original): The composition of claim 4, wherein said composition has a terminal blocking group.

Claim 6 (Previously presented): The composition of claim 4, wherein said composition has a terminal 9-fluoreneacetyl (Fa) group.

Claim 7 (Previously presented): The composition of claim 4, wherein said composition has a terminal 9-fluorenylmethoxycarbonyl (Fmoc) group.

Claim 8 (Canceled).

Claim 9 (Original): The composition of claim 1, wherein F¹ and F² are the same fluorophore.

Claim 10 (Original): The composition of claim 9, wherein said F¹ and F² have an excitation wavelength between about 315 nm and about 800 nm.

Claim 11 (Original): The composition of claim 1, wherein the F¹ molecule is attached through either an α -amino group of the aa¹ amino acid or through a side chain amino group of the aa¹ amino acid, or through a sulfhydryl group of a side chain of the aa¹ amino acid.

Claim 12 (Original): The composition of claim 1, wherein the F² molecule is attached either through a side chain amino group of the aa¹⁰ amino acid, through a carboxyl group of the aa¹⁰ amino acid, or through a sulfhydryl group of a side chain of the aa¹⁰ amino acid.

Claim 13 (Currently amended): The composition of claim 1, wherein said fluorophore is selected from the group consisting of rhodamine X, 9-(2,5-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide or other anion-(TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide or other anion-(TMR), 9-(2,5)-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion (Rh6G), 9-(2,6)-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion, π -9-(2,5-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,6-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), π -9-(2,5-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), 9-(2,6-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), carboxytetramethylrhodamine, carboxyrhodamine-X, diethylaminocoumarin, 9-(2,5-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (5-TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (6-TMR), 9-(2-carboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)xanthylium, and 9-(2-carboxyphenyl)-xanthylium.

Claim 14 (Original): The composition of claim 1, wherein said fluorophore comprises a carbocyanine dye.

Claim 15 (Previously presented): The composition of claim 9, wherein said composition bears a hydrophobic group.

Claim 16 (Original): The composition of claim 1, wherein said composition bears a hydrophobic group.

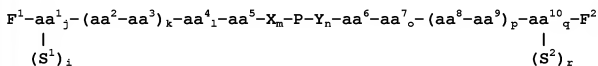
Claim 17 (Currently amended): The composition of claim 16, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group (Fa), 1-fluorene-carboxylic group, 9-fluorene-carboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), γ -Tosyl (Tos), 4,4-dimethoxybenzhydryl (Mbh), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-dioxacyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

Claim 18 (Original): The composition of claim 17, wherein said hydrophobic group is Fmoc.

Claim 19 (Original): The composition of claim 17, wherein said hydrophobic group is Fa.

Claim 20 (Original): The composition of claim 17, wherein said hydrophobic group is attached to the amino terminus of the molecule.

Claim 21 (Previously presented): A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



wherein, P is a peptide selected from the group consisting YVHDAPV (SEQ ID NO:216), and (dY)VHDAPV (SEQ ID NO:217);

F¹ and F² are fluorophores and F¹ is attached to the amino terminal amino acid and F² is attached to the carboxyl terminal amino acid;

S¹ and S², when present, are peptide spacers ranging in length from 1 to about 50 amino acids and S¹, when present, is attached to the amino terminal amino acid and S², when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

aa¹ and aa¹⁰ are independently selected from the group consisting of lysine, ornithine and cysteine;

-aa²-aa³-, and -aa⁸-aa⁹- are independently selected from the group consisting of an amino acid or a dipeptide where said amino acid or dipeptide consist of amino acids selected from the group consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

aa⁵, aa⁴, aa⁶, and aa⁷ are independently selected from the group consisting of proline, 3,4-dehydropyrrolidine, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, βAla-Gly, βAla-βAla, γAbu-Gly, βAla-γAbu, Gly-Gly-Gly, γAbu-γAbu, Ahx-Gly, βAla-Gly-Gly, Ahx-βAla, βAla-βAla-Gly, Gly-Gly-Gly-Gly (SEQ ID NO:211), Ahx-γAbu, βAla-βAla-βAla, γAbu-βAla-Gly, γAbu-γAbu-Gly, Ahx-Ahx, γAbu-γAbu-βAla, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, Gly-βAla, βAla-βAla, Gly-γAbu, γAbu-βAla, Gly-Gly-Gly, γAbu-γAbu, Gly-Ahx, Gly-Gly-βAla, βAla-Ahx, Gly-βAla-βAla, Gly-Gly-Gly-Gly (SEQ ID NO:211-214), γAbu-Ahx, βAla-βAla-βAla, Gly-βAla-γAbu, Gly-γAbu-γAbu, Ahx-Ahx, βAla-γAbu-γAbu, and Gly-Ahx-Ahx; and

when i is 1, S¹ is joined to aa¹ by a peptide bond through a terminal alpha amino group of aa¹; and when r is 1, S² is joined to aa¹⁰ by a peptide bond through a terminal alpha carboxyl group of aa¹⁰.

Claim 22 (Original): The composition of claim 21, wherein the carboxyl terminal amino acid in which the carboxylic acid group is replaced with an amide.

Claim 23 (Original): The composition of claim 21, wherein:

r is zero; and

aa¹⁰ has a C-terminal amide group or free carboxylic acid group.

Claim 24 (Previously presented): The composition of claim 21, comprising an amino acid sequence selected from the group consisting of KDBYVHDAPVPGY (SEQ ID NO:218),

KDBGYVHDAPVGPKGY (SEQ ID NO:219), KDBGYVHDAPVGJPKGY (SEQ ID NO:220), and KDBGJ(dY)VHDAPVGJPKGY (SEQ ID NO:221).

Claim 25 (Original): The composition of claim 24, wherein said composition has a terminal blocking group.

Claim 26 (Original): The composition of claim 24, wherein said composition has a terminal Fa group.

Claim 27 (Original): The composition of claim 24, wherein said composition has a terminal Fmoc group.

Claim 28 (Original): The composition of claim 21, wherein F^1 and F^2 are the same fluorophore.

Claim 29 (Original): The composition of claim 28, wherein F^1 and F^2 have an excitation wavelength between about 315 nm and about 800 nm.

Claim 30 (Original): The composition of claim 21, wherein the F^1 molecule is attached through either an α -amino group of the aa^1 amino acid or through a side chain amino group of the aa^1 amino acid, or through a sulfhydryl group of a side chain of the aa^1 amino acid.

Claim 31 (Original): The composition of claim 21, wherein the F^2 molecule is attached either through a side chain amino group of the aa^{10} amino acid, through a carboxyl group of the aa^{10} amino acid, or through a sulfhydryl group of a side chain of the aa^{10} amino acid.

Claim 32 (Currently amended): The composition of claim 21, wherein said fluorophore is selected from the group consisting of rhodamine X, 9-(2,5-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide or other anion-(TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide or other anion-(TMR), 9-(2,5)-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion (Rh6G), 9-(2,6)-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion, π -9-(2,5-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,6-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), π -9-(2,5-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), 9-(2,6-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh),

carboxytetramethylrhodamine, carboxyrhodamine-X, diethylaminocoumarin, 9-(2,5-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (5-TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (6-TMR), 9-(2-carboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)xanthylium, and 9-(2-carboxyphenyl)-xanthylium.

Claim 33 (Original): The composition of claim 21, wherein said fluorophore comprises a carbocyanine dye.

Claim 34 (Original): The composition of claim 21, wherein said composition bears a hydrophobic group.

Claim 35 (Currently amended): The composition of claim 34, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group (Fa), 1-fluorene-carboxylic group, 9-fluorene-carboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthy (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), γ -Tosyl (Tos), 4,4-dimethoxybenzhydryl (Mbh), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

Claim 36 (Original): The composition of claim 21, wherein said hydrophobic group is Fmoc.

Claim 37 (Original): The composition of claim 21, wherein said hydrophobic group is Fa.

Claim 38 (Original): The composition of claim 21, wherein said hydrophobic group is attached to the amino terminus of the molecule.

Claims 39-61 (Canceled).